

- (b) VVVVSTTGTGDPPDTARKFVKEI (SEQ ID NO: 53),
- (c) AHLRYGLLGLGDSEYTYFCNNGGKIIDKRL (SEQ ID NO: 54),
- (d) LQPRPYSCASSSLFHPGKL (SEQ ID NO: 55),
- (e) FVFNIVEFLSTATT (SEQ ID NO: 56),
- (f) LRKGVCTGWLALLVASV (SEQ ID NO: 57),
- (g) IPIIMVGPGTGIAPFIGFLQHR (SEQ ID NO: 58),
- (h) SFSRDA (SEQ ID NO: 59),
- (i) APAKYVQDNIQLHGQQVARILLQENGHIYVCGDAKNMAKDV
(SEQ ID NO: 60), or
- (j) KRYLQDIWS (SEQ ID NO: 61).

50-55 (Cancelled)

56. (New) A substantially pure nucleic acid molecule having at least 95% sequence identity to SEQ ID NO: 1 and encoding a mammalian methionine synthase reductase polypeptide, wherein said polypeptide is capable of catalyzing the reductive methylation of methionine synthase-cob(II)alamin to generate methionine synthase-cob(III)alamin-CH₃.

57. (New) The nucleic acid of claim 56, wherein said nucleic acid molecule has the sequence of SEQ ID NO: 1.

58. (New) The nucleic acid molecule of claim 56, wherein said nucleic acid molecule

encodes a human methionine synthase reductase polypeptide.

59. (New) The nucleic acid molecule of claim 56, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide having at least 20% of the methionine synthase reductase activity of the methionine synthase reductase polypeptide of SEQ ID NO: 2.

60. (New) The nucleic acid molecule of claim 59, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide having at least 55% of the methionine synthase reductase activity of the methionine synthase reductase polypeptide of SEQ ID NO: 2.

61. (New) The nucleic acid molecule of claim 56, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide that comprises a consensus binding site for one or more cofactors selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises any one of SEQ ID NOs: 25 or 52-61.

62. (New) The nucleic acid molecule of claim 56, wherein the polynucleotide sequence of said nucleic acid molecule comprises a naturally-occurring mutation or polymorphism present in a mammalian methionine synthase reductase gene.

63. (New) A substantially pure antisense nucleic acid molecule that hybridizes in 2X

SSC medium at 40°C to the polynucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, wherein said antisense nucleic acid molecule decreases the expression of methionine synthase reductase polypeptide.

64. (New) The antisense nucleic acid molecule of claim 63, wherein said nucleic acid molecule has a polynucleotide sequence completely complementary to at least 30 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

65. (New) A substantially pure antisense nucleic acid molecule having a polynucleotide sequence that is completely complementary to a polynucleotide sequence having at least 95% sequence identity to at least 18 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, wherein said antisense nucleic acid molecule decreases the expression of methionine synthase reductase polypeptide.

66. (New) The antisense nucleic acid molecule of claim 65, wherein said antisense nucleic acid molecule is completely complementary to at least 18 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

67. (New) The antisense nucleic acid molecule of claim 63 or 65, wherein said methionine synthase reductase polypeptide is a mutant or polymorphic methionine synthase reductase polypeptide.

68. (New) The antisense nucleic acid molecule of claim 63 or 65, wherein said antisense nucleic acid molecule comprises a polynucleotide sequence the complete complement of which comprises a naturally-occurring mutation or polymorphism present in a mammalian methionine synthase reductase gene.

69. (New) A substantially pure nucleic acid molecule having at least 95% sequence identity to SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47 and encoding a mammalian methionine synthase reductase polypeptide that has a reduced ability to catalyze the reductive methylation of methionine synthase-cob(II)alamin to generate methionine synthase-cob(III)alamin-CH₃ relative to the methionine synthase reductase activity of a mammalian methionine synthase reductase polypeptide encoded by SEQ ID NO: 1.

70. (New) The nucleic acid of claim 69, wherein said nucleic acid molecule has the sequence of SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47.

71. (New) The nucleic acid molecule of claim 69, wherein the polynucleotide sequence of said nucleic acid molecule comprises a naturally-occurring mutation or polymorphism present in a mammalian methionine synthase reductase gene.

72. (New) A substantially pure nucleic acid molecule produced by a method comprising:
(a) obtaining a nucleic acid molecule from a mammalian cell; and

(b) substantially purifying said nucleic acid molecule, wherein said nucleic acid molecule is naturally-occurring in said cell, has at least 90% sequence identity to SEQ ID NO: 1, and encodes a mammalian methionine synthase reductase polypeptide, wherein said polypeptide is capable of catalyzing the reductive methylation of methionine synthase-cob(II)alamin to generate methionine synthase-cob(III)alamin-CH₃.

73. (New) A substantially pure antisense nucleic acid molecule produced by a method comprising:

(a) obtaining a nucleic acid molecule from a mammalian cell, wherein said nucleic acid molecule has at least 90% sequence identity to SEQ ID NO: 1 and encodes a mammalian methionine synthase reductase polypeptide; and

(b) reverse-transcribing all or a portion of said nucleic acid molecule to generate an antisense nucleic acid molecule having a polynucleotide sequence that is completely complementary to a polynucleotide sequence having at least 95% sequence identity to at least 18 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 41, SEQ ID NO: 43, SEQ ID NO: 45, or SEQ ID NO: 47, wherein said antisense nucleic acid molecule decreases the expression of methionine synthase reductase polypeptide.

74. (New) The nucleic acid molecule of claim 72 or 73, wherein said nucleic acid molecule encodes a mammalian methionine synthase reductase polypeptide that comprises a consensus binding site for one or more cofactors selected from the group consisting of FAD, FMN, and NADPH, wherein said binding site comprises any one of SEQ ID NOs: 25 or 52-61.

75. (New) The nucleic acid molecule of claim 72 or 73, wherein the polynucleotide sequence of said nucleic acid molecule comprises a naturally-occurring mutation or polymorphism present in a mammalian methionine synthase reductase gene.